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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/837,138	PETRINI ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *the amendment filed July 29, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,20-22,26,27 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,20-22,26,27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/18/01+2/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. After review and reconsideration the finality of the rejection of June 29, 2004 is withdrawn.

2. Claims 5, 6, 20, 21, 22 and 26 have been amended. Claim 28 has been cancled. Claim 29 has been added. Claims 5, 6, 20-22, 26, 27, and 29 are pending and under consideration.

3. Text of sections of Title 35, U.S. Code not found in this action can be found in a previous action.

4. Claims 5, 6, 20-22, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A) As drawn to a vertebrate DNA repair polypeptide having a molecular weight of about 95000 Da as determined by SDS-PAGE.

Claims 26 and 27 are product claims drawn in part to a host cell comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a MW of "about" 95000 Da. Claims 5, 20, 21 and 22 are method claims reliant on the identity of an isolated nucleic acid comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a MW of "about" 95000 Da. The product claims encompass a genus of nucleic acid segments encoding a genus of polypeptides having a MW of about 95kDa. The specification describes only a single vertebrate polypeptide of 95kDa, as that of SEQ ID NO:2. The genus is highly variant comprising all homologs, mutants, allelic variants and orthologs having the approximate MW of 95kDa. The description of SEQ ID NO:2 does not adequately describe the claimed genus because the genus encompasses molecules which differ in structure from SEQ ID NO:2, and which differ in function from SEQ ID NO:2. The genus also encompasses molecules which differ in function from the instant SEQ ID NO:2 in that association with the Mre11/Rad50 complex is existent but altered in a quantitative or qualitative manner. Further, the association

with the Mre11/Rad50 complex does not determine the function of a mutant p95 protein in the cell because said mutant protein may retain the ability to associate with the Mre11/Rad50 complex, but have reduced or non-existent ability to transduce the DNA damage signal to said complex (see rejection under 103(a) below). Therefore, one of skill in the art would reasonably conclude that applicant was not in possession of the genus of p95 proteins at the time of filing and because applicant did not have possession of the claimed genus, it logically follows that method claims reliant on the claimed genus were also not in applicants possession.

(B) As drawn to a DNA segment comprising a complement of a portion of a nucleic acid segment.

Claims 26 and 27 and 28 are drawn in part to a complement of at least a portion of a nucleic acid segment encoding a vertebrate DNA repair polypeptide associated with the Mre11/Rad50 complex having a molecular weight of about 95000 Da. Claims 6 and 22 are method claims reliant on the identity of a complement of at least a portion of a nucleic acid segment encoding a vertebrate DNA repair polypeptide associated with the Mre11/Rad50 complex having a molecular weight of about 95000 Da. When given the broadest reasonable interpretation, the term "at least a portion" in reference to a complementary polynucleotide sequence can read on a portion as small as one nucleotide, therefor claims directed to nucleic acids comprising at least a portion of the complementary sequence are not limited by the structures of the complete complementary sequences to the polynucleotides encoding p95 or SEQ ID NO:2. Further, the functional qualification of being associated with the Mre11/Rad50 complex does not apply to the portion of the complement, but the coding sequence. In addition, the association of the protein with the Mre11/Rad50 complex cannot be construed as limiting the structure of the antisense sequence which is not a coding sequence because the claim requires a polynucleotide having only one nucleotide in common with the complete complement of the polynucleotides which encode SEQ ID NO:2. The specification provides a written description only for the polynucleotides encoding SEQ ID NO:2. The genus of nucleic acids encompassed by the claims is highly variant because said genus includes molecules which differ widely in both structure and function from the nucleic acids which are the complete complement of SEQ ID NO:2 because the complementary sequence need only minimally comprise a single nucleotide of the polyncuetides encoding SEQ ID NO:2. One of skill in the art would reasonably conclude

that applicant was not in possession of a genus of nucleic acids comprising at least a portion of the complement of the nucleic acid segment encoding SEQ ID NO:2 and method claims reliant on said genus.

Claims 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated bySundarraj et al (FEBS Letters, 1978, Vol. 85, pp. 47-51) as evidenced by the abstract of Crawford and Black, (Virology, 1964, Vol. 24, pp. 388-392) and Graessman and Graessman, ('The Transformation Capacity of Early SV40 Fragments', In: Cell Transformation, Celis and Graessman, Ed.s, 1984, pp. 113-126).

Claim 26 is drawn in part to an isolated transformed cell comprising an isolated nucleic acid molecule comprising a complement of at least a portion of a nucleic acid segment which encodes a vertebrate DNA repair polypeptide having a molecular weight of 95KDa and associate with the Mre11/Rad50 complex, wherein said nucleic acid molecule comprising a complement of at least a portion of the nucleic acid segment is operably linked to a promoter functional in the host cell. Claim 27 embodies the host cell of claim 26 which is a mammalian cell.

Sundarraj et al disclose the SV40 transformed human cell line GM637. The GM637 would contain the SV40 DNA and SV40 is an isolated DNA as evidenced by Crawford and Black,therefore the disclosure of Sundarraj et al meets the specific limitation of "a transformed cell comprising an isolated nucleic acid". SV40 is a DNA virus and therefore has a complementary sequence. Said complementary sequence present in the cells of the transformed GM637 would necessarily have at least one nucleic acid residue of the complementary sequence of SEQ ID NO:1 or the polynucleotides encoding SEQ ID NO:2 meeting the specific embodiment of claim 26 requiring a complement of at least a portion of the nucleic acid segment encoding a vertebrate DNA repair polypeptide with a MW of 95 KDa. The art (Graessman and Graessman, 'The Transformation Capacity of Early SV40 Fragments', In: Cell Transformation, Celis and Graessman, Ed.s, 1984, pp. 113-126, especially page 113, lines 4-9 under "Introduction") recognizes that the synthesis of the SV40 large T-antigen is required and sufficient for induction and maintenance of the transformed state. Therefore, the transformed cell line GM637 is expressing large T-antigen to maintain the transformed state and this fulfills

the specific embodiment of claim 26 which requires that the complement of a portion of the nucleic acid segment is operably linked to a promoter functional in the host cell.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 5, 6, 20-22, 26, 27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maser et al (Molecular and Cellular Biology, 1997, Vol. 17, pp. 6087-6096, reference of the IDS filed Apr 18, 2001) in view of Varon et al (Cell, 1998, Vol. 93, pp. 467-476) and Carney et al (Cell, 1998, Vol. 93, pp. 477-486).

Claim 5 is drawn to an in vitro method of altering the amount of a DNA repair polypeptide in a cell comprising providing a transformed host cell comprising an isolated nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a molecular weight of about 95000 Da operably linked to a promoter functional in the host cell, wherein the DNA repair polypeptide is associated with the Mre11/Rad50 complex and expressing the nucleic acid molecule in the transformed host cell as recombinant DNA repair polypeptide, wherein the amount of the recombinant polypeptide produced by the transformed cell is different than the amount of the DNA repair polypeptide produced by a corresponding

untransformed cell. Claim 6 is drawn to an in vitro method of altering the amount of a DNA repair polypeptide in a cell comprising providing a transformed host cell comprising a DNA segment comprising the complement of at least a portion of a nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a molecular weight of about 95000 Da operably linked to a promoter functional in the host cell wherein the DNA repair polypeptide is associated with the Mre11/Rad50 complex and expressing the DNA segment in the transformed host cell as antisense RNA so as to decrease the amount of the DNA repair polypeptide in the transformed cell.

Claims 20 and 21 are drawn to an in vitro method of altering the amount of a DNA repair polypeptide in a cell comprising providing a transformed host cell comprising an isolated nucleic acid molecule comprising a nucleic acid segment for a vertebrate DNA repair polypeptide having a molecular weight of about 95000 Da operably linked to a promoter functional in the host cell, wherein the DNA repair polypeptide is associated with the Mre11/Rad50 complex, and wherein the nucleic acid segment comprises SEQ ID NO:1 or the encodes SEQ ID NO:2 and expressing the nucleic acid molecule in the transformed host cell so as to alter the amount of the DNA repair polypeptide in the cell. Claim 22 embodies the method of claims 20 or 21 wherein the host cell is a mammalian cell.

Claim 26 is drawn in part to an isolated transformed host cell comprising an isolated nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a molecular weight of about 9500 Da or a complement of at least a portion of the nucleic acid segment, operably linked to a promoter functional in the host cell, wherein the DNA repair polypeptide is associated with the Mre11/Rad50 complex. Claim 29 embodies the method of claim 5 or 6 wherein the nucleic acid segment encodes SEQ ID NO:2.

Maser et al teach transformed human cell lines, GM637 and GM9607 which comprise the nucleic acids encoding Mre11, RAd50 and p95 (page 6092, Figure 8(b) and legend for Figure 8(b). Maser et al teach that the GM637 cell line is a normal human cell line and the GM9607 cell line is an AT cell line (page 6091, second column, lines 27-32). Maser et al note that irradiation of said cell lines does not change the level of Mre11 and Rad50 (Legend for Figure 8(b) "The hMre11-hRad50 complex is not altered by ionizing radiation") but that the formation of observable IRIF comprising hMre11/Rad50 at the site of DNA damage arising from the

irradiation was considerably reduced in AT cells (page 6091, second column, lines 27-36). Maser et al do not teach the GM637 and GM9607 cell lines transformed with a nucleic acid encoding p95 or the antisense of p95.

Varon et al teach the cDNA and the polypeptide of the instant SEQ ID NO:2 encoded therefrom (Figure 4). Varon et al term this polypeptide as "nibrin" . Varon et al teach that nibrin can form complexes with mre11 and Rad50 (page 474, first column, lines 13-17). Varon et al teach that AT has been hypothesized to arise from a defect in the processing of double strand breaks in DNA (page 474, first column, lines 10-13). Varon et al speculate that deficiencies in either the nibrin protein or the ATM protein disrupt a common pathway that functions to sense or repair double strand breaks in NBS and AT (page 474, first column, lines 17-20).

Carney et al suggest that the p95 protein is required for the relocalization of the hMre11/hRad50 complexes to the site of the double strand break in DNA and further hypothesizing that p95 regulates the hMre11/hRad50 complex by transducing a signal originating from the site of the DNA damage (page 482, first column, lines 10-16).

It would have been prima facie obvious at the time the invention was made to transform the GM9607 cell line with a nucleic acid encoding a functionally p95 protein in order to increase the level of the wild-type p95 protein in the cell and to transform the GM637 cell line with an anti-sense nucleic acid to p95 in order to decrease the level of the p95 protein in the normal cell. One of skill in the art would have been motivated to do so in order to determine if the restoration of the wild type p95 sequence would induce more IRIF formation at the site of DNA damage in AT cells and/or if elimination or decrease of the p95 sequence would reduce IRIF formation in the normal cells.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double-patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. In reBerg, 140 F.3d, 1428, 46 USPQ2d 1226 (Fed. Cir. 1998): In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993): In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

9. Claims 5, 6, 20-22, 26, 27 and 29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 20-24 and 26-28 of copending Application No. 09/837,602 in view of Varon et al (Cell, 1998, Vol. 93, pp. 467-476) and Carney et al (Cell, 1998, Vol. 93, pp. 477-486).

In the instant case the claims are anticipated by the claims of the '602 application in view of Varon et al and Carney et , the teachings of whom are set forth above. It would have been prima facie obvious at the time the invention was made to use the isolated and purified nucleic acid molecules and expression vectors of the '602 application in the methods of claims 5, 6, 20-22 because the nucleic acid encoding the vertebrate DNA repair polypeptide of SEQ ID NO:2 results in a polypeptide which has a molecular weight of 95KDa and is associated with the Mre11/Rad50 complex, as taught by Varon et al and Carney et al in the rejection set forth above..

This is a provisional obviousness-type double patenting rejection.

10. All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
3/31/2005

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER